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10/506,715	09/07/2004	Massimo Bresciani	EURA130518	4886

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EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,715	BRESCIANI ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-21* is/are pending in the application.

4a) Of the above claim(s) *16-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Note to Applicant: References to paragraphs in non-patent literature refer to full paragraphs (e.g. 'page 1 column 1 paragraph 1' refers to the first full paragraph on page 1 in column 1 of the reference)

Election/Restrictions

To summarize the restriction, applicant elected Group I with traverse for prosecution. Claims 16-21 were withdrawn from further consideration.

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquires of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lai et al. (previously cited) in view of Carli et al. (previously cited).

Lai et al. teach a method where a cross-linked biodegradable polymer is treated with a pure supercritical fluid (see abstract and claim 12; instant claim 1). Specifically, Lai et al. teach that the cross-linked polymers can be polysaccharides, as well as ordinary synthetic polymers (see column 3 lines 38-48; instant claim 8). In a particular embodiment, the cross-linked polymer is taught to be treated with pure (free form any drug) supercritical carbon dioxide for 1 hour (see column 5 lines 18-21; instant claims 1-3 and 7). Although, Lai et al. teach that the supercritical fluid treated cross-linked polymers of their invention are useful as drug delivery systems, they do not teach the steps necessary to produce such a device (see column 4 lines 38-39).

Carli et al. teach a method of impregnating a cross-linked polymer with a drug (making a drug delivery system) using a supercritical fluid (see abstract; instant claim 1). Specifically, Carli et al. teach the steps where the drug is dissolved in the supercritical fluid, then the cross-linked polymer is contacted with this drug containing fluid impregnating the polymer with the drug, then the supercritical fluid is removed resulting in a drug loaded cross-linked polymer (see page 2 lines 6-10; instant claim 1). Carli et al. go on to teach that the contacting of the drug loaded supercritical fluid can occur via a static and/or dynamic process for 15 minutes to 24 hours (see page 2 lines 22-26 and line 31-page 3 line 3; instant claims 4-6). The particular supercritical fluids taught for use in the process of Carli et al. include carbon dioxide, ethylene, propylene, and nitrous oxide (see page 2 lines 15-19; instant claim 7). Further, Carli et al. teach a collection of cross-linked polymers suitable for their process which include cross-linked polyvinyl pyrrolidone, cross-linked sodium carboxymethyl cellulose (interpreted as cross-linked cellulose), cross-linked sodium starch glycolate (interpreted as cross-linked starch), cross-linked polystyrene, and cross-linked acrylic acid, all of which fall into the categories of those taught by Lai et al. (see page 3 lines 17-22; instant claim 8).

It would have been obvious to one of ordinary skill in the art at the time of the invention to apply the supercritical fluid method of drug loading into a crosslinked polymer taught by Carli et al. in the method of Lai et al. One of ordinary skill in the art would have been motivated to make this combination because Carli et al. provide specific methods of product controlled release drug delivery systems, utilizing crosslinked polymers of the variety taught by Lai et al., which were known at the time of

the invention and part of a limited number of options. This combination would further have been obvious because it would allow for the use of the same solvent in polymer preparation and loading, streamlining the processing of the end product, and because the solvent is used in supercritical form, it would not add impurities that would require later removal. Since Lai et al. teach the use of the polymers produced by their method in drug delivery systems, this combination of references would result in the claimed method where a crosslinked polymer is treated (pre-treated) with a pure (free from any drug) supercritical fluid, then contacted with a supercritical fluid containing a dissolved drug, where the supercritical fluid is subsequently removed. Lai et al. in view of Carli et al. do not specifically teach that the drug precipitates inside the cross-linked polymer or the nature (amorphous character) of the drug. However, applicant's disclosure on page 2 of the specification states that the method of Carli et al. was employed by the applicant for the loading of drug via supercritical fluid (yielding precipitated drug in crosslinked polymer) and the desired characteristics (amorphous character) of the drug within the cross-linked polymer were attained (see instant specification page 2 lines 7-9 and 15-17). Further, since the method of impregnating the polymer with the drug taught by Carli et al. is the same as that claimed, the resulting structure would have the same properties as those claimed present in the product resulting from the claimed method. Thus the teachings of Lai et al. in view of Carli et al. meet the limitations of impregnated drug recited in instant claims 1 and 9. Therefore claims 1-9 are obvious over Lai et al. in view of Carli et al.

Claims 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lai et al. in view of Samain et al. (US Patent No. 5,736,371)

Lai et al. teach a method where a cross-linked biodegradable polymer is treated with a pure supercritical fluid after a crosslinking reaction is performed (see abstract and claim 12; instant claim 10). Specifically, Lai et al. teach that the cross-linked polymers can be polysaccharides, as well as ordinary synthetic polymers (see column 3 lines 38-48; instant claim 10). In a particular embodiment, the cross-linked polymer is taught to be treated with pure supercritical carbon dioxide for 1 hour (see column 5 lines 18-21; instant claims 11-14). Although, Lai et al. teach that the supercritical fluid treated cross-linked polymers of their invention are useful as drug delivery systems, Lai et al. do not teach starch or cellulose as particular polysaccharides.

Samain et al. teach biodegradable polymers envisioned for use in drug delivery (see column 1 lines 6-8). Samain et al. go on to teach cross-linked cellulose and cross-linked starch as particular biodegradable polymers of the invention (see column 2 lines 64-66; instant claim 10).

It would have been obvious to one of ordinary skill in the art to select starch or cellulose, as taught by Samain et al, for the particular polysaccharides used in the method of Lai et al. since they were known for use in crosslinked form in drug delivery devices and Lai et al. teach the crosslinked polymer product of their method in drug delivery devices. Therefore claims 10-14 are obvious over Lai et al. in view of Samain et al.

Response to Arguments

Applicants' arguments, filed May 4, 2009, have been fully considered but they are not deemed to be persuasive regarding the rejections under 35 USC 103(a).

Regarding rejection under 35 USC 103(a) over Lai et al. in view of Carli et al.:

Applicant argues that neither Lai et al. nor Carli et al teach contacting a cross-linked polymer with supercritical fluid free from any drug as a pretreatment for drug loading. Lai et al. implicitly teaches this limitation when they teach the use of the cross-linked materials that their method yields in controlled drug delivery systems and that their method includes a step of treating a crosslinked polymer with pure supercritical fluid (see column 2 lines 31-38 and column 5 lines 13-21). Here, the pure supercritical fluid treatment after the cross-linking reaction would constitute a “pre-treatment” step since Lai et al. envision their end product for drug delivery systems. Furthermore, it is not necessary that the prior art employ the same reasoning as the instant applicant in order to reach the same result as instantly claimed (see MPEP 2144 IV). In either case, the teachings of Lai et al. are sufficient to establish that the claimed “pretreatment” step was known in the art at the time of the invention. Applicant further argues that a motivation to combine the cited references was not provided. The rejection explained a motivation for combining the references by the discussion of the teachings of Carli et al. on the method of loading a crosslinked polymer with a supercritical fluid being known at the time of the invention and within the ordinary capabilities of one of ordinary skill in the art. Applicant even refers to this methodology as “standard” (see instant specification

page 2 lines 18-21). One of ordinary skill in the art would have been motivated to use a known "standard" method to load a drug into a crosslinked polymer simply because it was known and "standard". Thus the use of the method of Carli et al. to produce the controlled release drug delivery system generally taught by Lai et al. would have been obvious at the time of the invention. Applicant goes on to argue that all the limitations of Lai et al. were not considered, but does not expound upon any particular limitations or what relevance they have to the rejection.

Regarding presentation of unexpected results:

Applicant reiterates examples in the instant specification that were referenced as demonstrating unexpected results.

Applicant notes that no relevance was given to the particular kind of polymer/drug/fluid in the examples because the combination was the same within each single evaluation. While in the context of a single example this lack of concern is understood, in as much as the examples are demonstrative of the entire invention, it is not clear that the examples represent the breadth of the invention. Berens et al. does still raise a valid issue for the instant invention regarding the variations (which could include negation of the "unexpected result") that can be seen in loading depending on the polymer/drug combination employed. For instance, if a polymer and drug that carry a positive charge were employed in the claimed method, it is not clear that the invention would have the same result as if both were uncharged as in the examples. Thus the scope of the claims and the examples that are relied upon to demonstrate unexpected

results are not commensurate in scope because the results cannot be extrapolated to the full breadth of the claims.

Applicant argues that Domingo is not relevant to the instant invention because it does not address crosslinked polymers; however, the process of using supercritical fluids to load additives into polymers was established in non-crosslinked polymers prior to the work by Carli et al. teaching that the process is also applicable in crosslinked polymers (see Carli et al. page 1 lines 24-31). Since the same process was known both for crosslinked and non-crosslinked polymers, it would be reasonable to expect that the same trends in behavior (e.g. loading increasing with increasing temperature at constant pressure, material and exposure time) would be seen in both.

While applicant has demonstrated some instances where the instantly claimed method yields a different product than a similar method with no pretreatment step, applicant has not established the expected result for the invention. Applicant attributes the differences in end result in these comparisons to the presence or absence of a pre-treatment step; however, the discussions do not address the additional variable of supercritical fluid exposure time. The overall treatment time in the reference sample as compared to the invention sample is different in each example. While applicant touts this difference as an advantage of the invention, it is not clear if the same result would also occur had the treatment times been the same. Therefore the discussion of unexpected results is not persuasive.

Regarding rejection under 35 USC 103(a) over Lai et al. in view of Samain et al.:

Applicant argues that Lai et al. does not teach a method of increasing the drug-loading capacity of a cross-linked polymer that includes treating the cross-linked polymer with a supercritical fluid that does not contain any drug and that Samain et al. does not cure this deficiency. As discussed in the rejection and the arguments above, Lai et al. teaches the claimed method steps of treating a crosslinked polymer with a supercritical fluid free of drugs. While Lai et al. does not explicitly teach particular polysaccharide polymers, since they envision their end product in drug delivery devices and Samain et al. teach particular crosslinked polysaccharides that were known for use in drug delivery devices, it would have been obvious to one of ordinary skill to select one of this finite set of particular polysaccharides taught by Samain et al. Therefore Lai et al. in view of Samain et al. make obvious the claimed method.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Thursday 8-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

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